GLYCYL-L-GLUTAMINE ANTAGONIZES α-MSH ELICITED THERMOGENESIS IN PGE_2-SENSITIVE mPOA SITES. G.E. Resch and W.R. Millington, Div. Mol. Biol. & Biochem., Univ. Missouri-Kansas City, Kansas City, MO.

Glycyl-L-glutamine (β-endorphin$_{30-31}$) is synthesized through the post-translational endoproteolysis of β-endorphin-1-31. The biological activity spectrum of glycyl-L-glutamine has not been extensively evaluated, although earlier studies showed that glycyl-L-glutamine antagonizes the behavioral actions of both β-endorphin and α-melanocyte-stimulating hormone (α-MSH), which is co-synthesized with β-endorphin from a common precursor, pro-opiomelanocortin (POMC). The objective of the present experiments was to evaluate whether glycyl-L-glutamine modulates the thermoregulatory actions of α-MSH. To examine this question, we injected α-MSH and/or glycyl-L-glutamine through a guide cannula previously implanted in the medial preoptic area (mPOA) 0.5 mm lateral and 7 mm ventral to bregma. Thermoregulatory mPOA sites were identified, based on their response to PGE_2, by injecting PGE_2 (1 .) through a 29 gauge cannula lowered through the guide cannu. .2 mm stepwise increments until a rise in colonic temperature (Tc) was detected. α-MSH (0.6 nmol) injection into PGE_2 sensitive mPOA sites generated a hyperthermic response, inducing a 0.64 ± 0.17 °C (mean ± SE; n = 6) rise in Tc within 45 min. Co-administration of glycyl-L-glutamine (3.0 nmol) completely blocked the response to α-MSH, maintaining Tc at baseline levels (Tc change = 0.0 ± 0.02 °C; n = 6; $P < 0.01$). The inhibitory response did not result from glycyl-L-glutamine hydrolysis because co-administration of its constituent amino acids, glycine and glutamine, had no effect whatsoever on the α-MSH-induced rise in Tc. Neither saline nor glycyl-L-glutamine injection alone into mPOA PGE_2 sensitive thermoregulatory sites elicited a significant Tc response. These data demonstrate that glycyl-L-glutamine antagonizes the thermoregulatory actions of α-MSH, and together with earlier reports, further suggest that the dipeptide acts as an inhibitory modulator of other peptides co-released from POMC neurons. (Supported by USAMRDC grant DAMD17-90-Z-0022)